Amended claims

1. Use of at least one murine genomic region involved in the development of cancer selected from the group consisting of: Adam11, AI462175, Cd24a, Edg3, Itgp, Kcnj16, Kcnk5, Kcnn4, Ly108, Ly6i, mouse homologue of EMILIN, Mrc1, Ninj2, Nphs1, Sema4b, Tm9sf2, and Tnfrsf17, encoding cell surface proteins; Apobec2, Btd, Cds2, Clpx, Ddx19, Ddx21, Dnmt2, Dqx1, Hdac7a, Lce-pending, Mgat1, mouse homologue of CILP, mouse homologue of NOH61, Nudel-pending, Pah, Pdi1, Ppia, Prps1, Ptgds, and Vars2, encoding enzymes; Dagk4, mouse homologue of PSK, Nme2, Snf1lk and Tyki, encoding kinases; Inpp4a and Inpp5b, encoding phosphatases; Il16, Prg, and Scya4, encoding secreted factors; Akap7, Api5, Arfrp1, Arhgap14-pending, Cish2, Dapp1, Fabp6, Fkbp8, Fliz1-pending, Hint, Ier5, Jundp2-pending, Lmo6, Mid1, mouse homologue of AKAP13, mouse homologue of BIN2, mouse homologue of CEZANNE, mouse homologue of CHD2, mouse homologue of MBLL, mouse homologue of SLC16A10, mouse homologue of SLC16A6, mouse homologue of SLC17A5, mouse homologue of TAF5L, mouse homologue of U1SNRNPBP, mouse homologue of ZNF8, Mtap7, Myo1c, Nkx2-3, Nsf, Pcdh9, Pkig, Prdx2, Pscd1, Psmb1, Psme1, Psme2, Rgl1, Ril-pending, Sax1, Slc14a2, Slc7a1, Slc7a11, Swap70, Txnip, and Ubl3, encoding signaling proteins; Clic3, Gtl1-13, mouse homologue of NOL5A, and Vdac2, encoding structural proteins; ABT1-pending, Ctbp1, Dermo1, Ebf, Elf4, Ldb1, mouse homologue of NR1D1, mouse homologue of ZER6, Rest, Tbp, Zfp238, Zfp287, and Zfp319, encoding proteins involved in transcriptional regulation; Lrrc2, Satb1, Slfn4, and genomic regions with the following Celera identification codes mCG10290, mCG10613, mCG11234, mCG11325, mCG11355, mCG11803, mCG11817, mCG12566,

mCG12630, mCG12824, mCG13346, mCG14143, mCG14155, mCG14342, mCG15141, mCG15321,, mCG16761, mCG16858, mCG17127, mCG17140, mCG17142, mCG17547, mCG17569, mCG17751, mCG17799, mCG17802, mCG17918, mCG18034,, mCG1850, mCG18663, mCG18737, mCG20276, mCG20905, mCG20994, mCG21403, mCG21505, mCG21529, mCG21530, mCG21803, mCG22014, mCG22045, mCG22386, mCG2258, mCG22772, mCG23032, mCG23035, mCG23069, mCG23075, mCG23120, mCG2543, mCG2824, mCG2947, mCG3038, mCG3729, mCG3760, mCG50409, mCG50651, mCG5068, mCG5070, mCG51393, mCG52252, mCG52498, mCG53009, mCG53724, mCG55023, mCG55075, mCG55198, mCG55265, mCG55512, mCG56069, mCG56089, mCG56746, mCG57132, mCG57265, mCG57617, mCG57827, mCG58254, mCG58345, mCG5900, mCG5905, mCG59368, mCG59375, mCG59533, mCG59662, mCG59810, mCG59997, mCG60526, mCG60833, mCG61221, mCG61661, mCG61897, mCG61907, mCG61943, mCG62177, mCG62971, mCG63537, mCG63601, mCG64346, mCG64382, mCG64398, mCG65022, mCG65585, mCG65785, mCG66128, mCG66379, mCG66776, mCG66965, mCG7831, mCG7856, mCG8424, mCG9002, mCG9537, mCG9538, mCG9791, mCG9792, mCG9843, mCG9875, mCG9877, and mCG988, or their human homologue for the preparation of polypeptide encoded by said region.

2. Use of at least one murine genomic region listed in claim1 or its human homologue for the preparation of an inhibitor capable of inhibiting the transcription product or activity of a polypeptide encoded by said region or affected by transformations in said region.

3. Use according to claim 2, wherein said inhibitor is a small molecule interfering with the biological activity of the polypeptide encoded by said genomic region or with the biological activity of a polypeptide the expression of which is affected by transformations in said genomic region.

4. Use according to claim 2, wherein said inhibitor is an antibody.

5. Use according to claim 2, wherein said inhibitor is an antisense

molecule, in particular an antisense RNA or antisense oligodeoxynucleotide.

6. Use according to claim 2, wherein said inhibitor is an RNAi molecule.

7. Use according to claim 2, wherein said inhibitor is a ribozyme.

8. Isolated nucleic acid sequence comprising at least one murine genomic region listed in claim 1 or its human homologue.

9. Isolated nucleic acid sequence according to claim 8, further comprising one or more regulatory sequences.

10. Recombinant vector comprising the nucleic acid sequence of claim 8 or 9.

11. Recombinant host cell comprising the vector of claim 10.

12. Recombinant host cell according to claim 11, wherein said host cell is a eukaryotic host cell

13. A eukaryotic host cell according to claim 12, wherein said eukaryotic host cell is a mammalian stem cell.

14. A mammalian stem cell according to claim 13, wherein said mammalian stem cell is a hematopoietic stem cell.

15. Inhibitor compound capable of inhibiting the transcription product or polypeptide encoded by at least one murine genomic region listed in claim 1 or its human homologue or capable of inhibiting the transcription product or polypeptide the expression of which is affected by a transformation in said genomic region.

16. Inhibitor compound according to claim 15, wherein said inhibitor compound is an antibody or derivative thereof directed against said polypeptide.

17. Inhibitor compound according to claim 16, wherein said polypeptide is expressed on the cell membrane.

18. Inhibitor compound according to claim 16 or 17, wherein said derivative is selected from the group consisting of scFv fragments, Fab fragments, chimeric antibodies, bifunctional antibodies, intrabodies, and other antibody-derived molecules.

19. Inhibitor compound according to claim 15, wherein said inhibitor

compound is a small molecule interfering with the biological activity of said polypeptide.

20. Inhibitor compound according to claim 15, wherein said inhibitor compound is an antisense molecule, in particular an antisense RNA or antisense oligodeoxynucleotide.

21. Inhibitor compound according to claim 15, wherein said inhibitor compound is an RNAi molecule.

22. Inhibitor compound according to claim 15, wherein said inhibitor compound is a ribozyme.

23. Inhibitor compound according to any one of the claims 15-22, for use in the treatment of cancer.

24. Inhibitor compound according to claim 23, wherein said cancer is leukemia, preferably acute myeloid leukemia (AML).

25. Use of an inhibitor compound according to any one of the claims 15-24, for the preparation of a pharmaceutical composition for the treatment of cancer.

26. Use according to claim 25, wherein said cancer is leukemia, preferably acute myeloid leukemia (AML).

27. Use according to claim 25 or 26, wherein the treatment comprises gene therapy.

28. Use of an inhibitor compound according to any one of the claims 15-22, for the preparation of a pharmaceutical composition for treatment of inflammatory diseases.

29. Pharmaceutical composition for the treatment of cancer, comprising at least one inhibitor compound according to any one of the claims 15-24 and a suitable excipient, carrier or diluent.

30. Method of treating a mammal, comprising administering to a mammal the pharmaceutical composition of claim 29 in an amount effective to alleviate or prevent the formation of cancer, preferably in an amount effective to provide remission or prevention of relapse of solid tumors.

31. Method according to claim 30, wherein said cancer is leukemia,

preferably acute myeloid leukemia.

32. Method of treating a mammal, comprising administering to a mammal the hematopoietic stem cell of claim 14 in an amount effective to alleviate or prevent the formation of leukemia, preferably acute myeloid leukemia.

33. Use of at least one murine genomic region listed in claim 1 or its human homologue or a transcription product thereof or polypeptide encoded thereby for the preparation of a diagnostic reagent for diagnosis of cancer.

34. Use according to claim 33, wherein said cancer is leukemia, preferably acute myeloid leukemia (AML).

35. A diagnostic reagent capable of specifically binding to a murine genomic region listed in claim 1 or its human homologue or a transcription product thereof or polypeptide encoded thereby.

36. A diagnostic reagent, according to claim 35, wherein said diagnostic reagent is an antibody or a derivative thereof.

37. A diagnostic reagent, according to claim 35 or 36, wherein said diagnostic reagent is a nucleic acid probe.

38. A diagnostic composition comprising a diagnostic reagent according to any one of claims 35-37.

39. Use of a diagnostic composition according to claim 38, for the diagnosis of cancer.

40. Use according to claim 39, wherein said cancer is a solid tumor of lung, colon, breast, prostate, ovarian or pancreas cancer.

41. Use according to claim 39, wherein said cancer is leukemia, preferably acute myeloid leukemia (AML).

42. Use according to any one of claims 39-41, wherein the diagnosis is performed by means of histological analysis of tissue specimens using specific antibodies directed against encoded polypeptides, using in-situ hybridisation analysis of gene expression levels in tissue specimens with RNA probes directed against gene sequences or using polynucleotide or oligonucleotide arrays.

43. A kit of parts for implementing a use of any one of claims 39-41,

comprising diagnostic composition according to claim 38, and one or more reagents selected form the group consisting of reagents for the isolation of nucleic acid fragments from a sample, reagents for the isolation of polypeptides from a sample, reagents for immunostaining of a sample, reagents for in situ hybridisation of a sample and reagents for performing nucleic acid array hybridisations.

44. Method for the development of an inhibitor compound according to any one of the claims 15-22, comprising the steps of:

a) identification of genes involved in cancer, in particular by using retroviral insertional tagging, optionally in a specific genetic background;

b) validation of one or more of the identified genes as potential target gene(s) for the inhibitor compound by one or more of the following methods:

- confirmation of the identified gene by Northern Blot analysis in cancer cell-lines;
- determination of the expression profile of the identified gene in tumors and normal tissue;
- determination of the functional importance of the identified genes for cancer;

c) production of the expression product of the gene; and

d) use of the expression product of the gene for the production or design of an inhibitor compound.

45. Method as claimed in claim 44, wherein the gene identified in step a) is a murine genomic region listed in Table 1 or its human homologue.

46. Method for the identification of genomic regions involved in the development of cancer comprising the steps of:

a) performing retroviral insertional mutagenesis of a subject, comprising infecting said subject with a tumor inducing retrovirus;

b) isolating chromosomal DNA from tumors developed in the infected subject;

c) digesting said chromosomal DNA with a restriction enzyme capable of cutting at least once in the DNA sequence of said tumor inducing retrovirus and at least once in the chromosomal DNA of said subject;

d) ligating the digested DNA to circular DNA;

e) amplifying the chromosomal DNA fragment flanking the retroviral DNA sequence by performing a first PCR reaction with said circular DNA using a first set of retrovirus-specific primers and performing a second nested PCR with the product of said first PCR reaction using a second nested set of retrovirus-specific primers, and

f) directly determining the nucleotide sequence of said chromosomal DNA fragment, and optionally comparing said nucleotide sequences with known sequences in a database to yield the genomic region involved in the development of cancer.

47. Method for the identification of common virus integration sites in the development of cancer comprising the steps of

a) performing the method of claim 46;

b) designing genomic region-specific amplification primers;

c) isolating nucleic acids from at least two tumors to be analysed for the presence of a common virus integration site;

d) performing an amplification reaction with said nucleic acids using a set of nested primers comprising genomic region-specific primers and retrovirus-specific primers, and

e) blotting the amplification products and separately hybridizing the resulting blot with a retrovirus-specific probe and a genomic region-specific probe to determine the presence of common virus integration sites between said tumors.

48. Set of genomic regions obtainable by a method according to claim 46 or 47.

49. Set of genomic regions according to claim 48, wherein said genomic regions are the murine genomic regions listed in Table 1.

50. Set of genomic regions according to claim 49, comprising at least 2, murine genomic regions selected from the group consisting of Adam11, Akap7, Arpgap14 , Bomb, Cd24a, Cish2, Cig5, Clic3, Cra, Dermol, EMILIN, Flj20489, Galnt5, Hook, Ier5, IL16, Iprg1, Itgp, Kcnk5, lrrc2, Ltb, Mbll, Mrc1, Mtap7, Ninj2, Nr1d1, Pcdh9, Prdx2, Prps1, Pdi1, Ptgd3, Rgl1, Sardh, Scya4, Slc16A6,

Swap70, Txnip, Trim46, Tnfrsf17 and Ub13.

51. Set of genomic regions according to claim 49, comprising at least 2, murine genomic regions selected from the group consisting of Cd24a, Cish2, Cra, Ltb and Prdx2.